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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,462	10/18/2005	Gordon Weingarten	PG4894USW	4839

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/524,462	WEINGARTEN ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment, which included cancellation of claims 15, 18, 19, addition of new claims 20-22 and amendment to claims 2-14 and 16-17, filed on 2/14/2005, is made of record.

Claims 1-14, 16-17 and 20-22 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed 2/14/2005, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 12-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same indefiniteness.

1. Recitation of A as "5 or 6-membered hetero aryl" without defining intended hetero atoms and their numbers, renders claim 1 and its dependent claims 2-10 and 12-22 indefinite as it is not clear what is the structural make-up of the heteroaryl.
2. Also in claim 1, in the definition of B, the choices 2, 3, 5 and 6 include an "•" in the ring at the point of attachment which renders claim 1 and its dependent claims indefinite as it is not clear what is intended. Normally, an "•" is used

indicate a chiral carbon. It is not clear whether it is intended for specific chiral form and the other form is not desired along with the racemate. If so it is not clear which form is intended.

3. Claim 10 is indefinite as it refers to examples 1 to13 without providing them. It is not clear what these examples are. See

4. Claims 12 and 13 are indefinite for more than one reason. First of all, claim12 and recite a formula III but the variable groups R^3 and R^4 are not defined in claim12 and claim 13 defines only the R^3 group. Secondly, the second process step B in both these claims are cryptic. It is not clear what is being converted to what and using what process. In addition, claim 13 which is dependent on compound of claim 2 now refers to compound of formula I which is recited in claim 1. Claim 13 is an improper dependent claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 17, 21 and 22 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating arthritis, does not reasonably provide enablement for treating any or all condition mediated by COX-2 as well as treating any or all inflammatory disorder generically embraced in the claim language. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. Following apply.

The instant method of use claims 15, 17, 21 and 22 are drawn to treating a condition mediated by COX-2 and treating an inflammatory disorder in general. Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of COX-2 by the instant compounds, claims 15, 17, 21 and 22 reach through treating any or all conditions and any or inflammatory disorder in general and thereby they lack adequate written description and enabling disclosure in the specification. From the reading of specification pages 7-10, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of cyclooxygenase COX-2, would be useful for all sorts of diseases including various inflammatory diseases, cancer, Parkinson's, various arthritis, multiple sclerosis etc. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended mammal. Moreover many if not most of diseases such as multiple sclerosis, Alzheimer's disease etc. are very difficult to treat and hardly possible to prevent as claimed herein. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition". There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties

since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

The scope of the claims include not only treatment but also prevention of a disease which is not adequately enabled solely based on the activity of the compounds as inhibitors of cyclooxygenase COX-2. "To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

No compound has ever been found to inhibit any or all reverse transcriptase and to treat diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine.

Next, applicant's attention is drawn to the Revised Utility and Written Description

Guidelines, at 66 FR 1092-1099, 2001, wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. The state of the art provides that COX-2 inhibitors inhibit production of prostaglandins that cause pain and swelling in arthritis. See http://www.medterms.com/script/main/Art.asp?ArticleKey=7098. Applicants have not provided any such nexus correlating the COX-2 inhibition activity and the treatment of any or all diseases or disorders generically embraced in the instant claims. See Freston, American Journal of Medicine 107(6A): 79S-89S, 1999, as well as Naesdal et al., European Journal of Gastroenterology & Hepatology 13(12): 1401-1406, 2001. Freston states that the uncertainty of the activity of COX-2 inhibitors. "The clinical consequences, if any of these effects remain to be determined in long-term studies in human". Also Naesdal et al., concluded that "The experience with COX-2 selective NSAIDs still limited and it remains to be studied whether a subpopulations of COX-2 selective NSAID users will benefit from gastro-duodenal protection", indicating the unpredictability in the activities of the function of COX-2 inhibitors.

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of

experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

1) The nature of the invention: Therapeutic use of the compounds in treating or preventing all diseases due to inhibition of cyclooxygenase COX-2 activity.

2) The state of the prior art: Although there are several, cyclooxygenase inhibitors known, they have not prevented or able to treat all diseases embraced in the instant claims. See Freston and Naesdal et al. cited above.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'preventive' effect of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There is no supporting evidence that all diseases embraced are treatable and even preventable in view of their inhibititory activity of cyclooxygenase COX-2.

6) The breadth of the claims: The instant claims embrace not only treatment but also the prevention of diseases.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards 'preventing' the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from

8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

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11/23/2005